

Application No. 10/696,391
Amendment dated September 24, 2007
Request for Continued Examination of October 31, 2007

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Docket No.: 47624CIP(71417)

AMENDMENTS TO THE CLAIMS

The below listing of claims will replace all prior versions, and listings, of claims in the application:

1-48. (canceled)

49. (Previously presented) A method for inducing new blood vessel growth in myocardial tissue of a mammal in need of such treatment comprising:

- a) administering an effective amount of a nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue;
- b) administering to the mammal an effective amount of at least one angiogenic factor or an effective fragment thereof, thereby inducing the new blood vessel growth in the myocardial tissue of the mammal, and increasing the frequency of endothelial progenitor cells (EPC) in the mammal; and
- c) monitoring a cardiac function by echocardiography, ventricular end-diastolic dimension (LVEDD), end-systolic dimension (LVESD), fractional shortening (FS), wall motion score index (WMSI), electromechanical mapping, cardiac angiography or LV systolic pressure (LVSP), wherein the method improves said cardiac function.

50. (Original) The method of claim 49, wherein the angiogenic factor is a vascular endothelial growth factor (VEGF) or an effective fragment thereof.

51. (Previously presented) The method of claim 50, wherein the VEGF is selected from the group consisting of VEGF-1, VEGF165, VEGF-B, VEGF-C, VEGF-2, and VEGF-3.

52. (Original) The method of claim 49, further comprising expressing the angiogenic protein or fragment in the myocardium.

53. (Canceled)

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53. (Canceled)

54. (Previously presented) The method of claim 49, wherein the increase in frequency of the EPC is at least about 20% as determined by a standard EPC isolation assay.

55. (Original) The method of claim 49, wherein the method further comprises increasing EPC differentiation in the mammal.

56. (Original) The method of claim 55, wherein the increase in EPC differentiation is at least about 20% as determined by a standard EPC culture assay or a standard hindlimb ischemia assay.

57. (Original) The method of claim 50, wherein the level of VEGF or VEGF fragment expression is sufficient to increase neovascularization by at least about 5% as determined by a standard cornea micropocket assay.

58. (Currently amended) The method of claim 49, wherein the administered angiogenic factor is stem cell factor (SCF), colony stimulating factor (CSF) or a fragment thereof is sufficient to increase ~~EPC~~ bone marrow derived EPC incorporation into foci.

59. (Currently amended) The method of claim 58, wherein the ~~EPC~~ bone marrow derived EPC incorporation into foci is at least about 20% as determined by a standard rodent bone marrow (BM) transplantation model.

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62. (Original) The method of claim 61, wherein the anti-coagulant is one or more of urokinase, plasminogen activator, and heparin.

63. (Original) The method of claim 49, wherein the nucleic acid is directly injected with a catheter or stent.

64. (Original) The method of claim 49, wherein the nucleic acid is inserted into a cassette operably linked to a promoter.

65. (Original) The method of claim 49, wherein the myocardial tissue is ischemic or is associated with infarction or dysfunction.

66-67. (Canceled)

68. (Previously presented) The method of claim 49, wherein the angiogenic protein or factor is one of acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF-1), VEGF165, epidermal growth factor (EGF), transforming growth factor α and β (TGF- α and TGF- β), platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), granulocyte/macrophage CSF (GM-CSF), stem cell factor (SCF), angiopoietin-1 (Ang1), nitric oxide synthase (NOS); or a mutein or fragment thereof.

69. (New) A method for inducing new blood vessel growth in myocardial tissue of a mammal in need of such treatment comprising:

- a) administering an effective amount of a nucleic acid encoding VEGF or an effective fragment thereof into the myocardial tissue;
- b) administering to the mammal an effective amount of GM-CSF, SCF, or an effective fragment thereof, thereby inducing the new blood vessel growth in the myocardial tissue of the mammal, and increasing the frequency of endothelial progenitor cells (EPC) in the mammal; and

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- c) monitoring a cardiac function by echocardiography, ventricular end-diastolic dimension (LVEDD), end-systolic dimension (LVESD), fractional shortening (FS), wall motion score index (WMSI), electromechanical mapping, cardiac angiography or LV systolic pressure (LVSP), wherein the method improves said cardiac function.

70. (New) A method for inducing new blood vessel growth in myocardial tissue of a mammal in need of such treatment comprising:

- a) administering an effective amount of a nucleic acid encoding VEGF-2 into the myocardial tissue;
- b) administering to the mammal an effective amount of GM-CSF, and SCF, thereby inducing the new blood vessel growth in the myocardial tissue of the mammal, and increasing the frequency of endothelial progenitor cells (EPC) in the mammal; and
- c) monitoring a cardiac function by echocardiography, ventricular end-diastolic dimension (LVEDD), end-systolic dimension (LVESD), fractional shortening (FS), wall motion score index (WMSI), electromechanical mapping, cardiac angiography or LV systolic pressure (LVSP), wherein the method improves said cardiac function.